

Amendments to the Claims

Listing of Claims:

Claims 1 - 57.

Claim 58 (new). A process for the cultivation and stimulation of three-dimensional, vital and mechanically-resistant cell transplants in a GMP-conform bioreactor, the process which comprises the following steps:

a) taking explant cells from an organism and preparing the explant cells for bioreactor cultivation and mixing a carrier matrix comprising commercially-available biocompatible, absorbable or autologous or homologous materials to form a cell matrix suspension;

b) placing the cell matrix suspension in a, optionally foiled, seeding piston having a cross-section adapted to a later transplant, and hardening or polymerizing therein;

c) optionally loading, with minimum pressure by way of an exactly fitting, inert stamp that is optionally structured or foiled;

d) inserting the seeding piston with the transplant into a chamber space of the bioreactor body;

e) medially placing the transplant from the seeding piston on the floor of the bioreactor, removing the seeding piston, and closing the bioreactor;

f) further cultivating the transplant by feeding a perfusion flow, and during the cultivation phase loading the transplant to a load pressure on a surface thereof opposite the floor of the bioreactor; and

g) after a completion of the cultivation, removing the replacement tissue material for further use.

Claim 59 (new). The process according to claim 58, which comprises subjecting the transplant to a load with a stamp applying pressure.

Claim 60 (new). The process according to claim 58, which comprises selectively controlling a blending in the bioreactor chamber due to the perfusion flow and the load pressure with regard to time and quantity or density in relation to the cultivation conditions.

Claim 61 (new). The process according to claim 58, wherein the transplant has conditioned cultivating medium flow through it at intervals and is subjected to loading in cycles with the load pressure.

Claim 62 (new). The process according to claim 58, which comprises subjecting the transplant to the load pressure during the perfusion flow.

Claim 63 (new). The process according to claim 58, which comprises stimulating the transplant in accordance with its use with static pressure loads, with in-vivo-simulating pressure loads or construct deformations, or with continuous-load intermittent or dynamic pressure forces.

Claim 64 (new). The process according to claim 58, which comprises applying the mechanical load with a frequency exceeding 0.1 Hz.

Claim 65 (new). The process according to claim 58, which comprises subjecting the transplant to mechanical pressure stimulation in the form of a symmetrical or asymmetrical half cosine or sine wave.

Claim 66 (new). The process according to claim 59, which comprises providing a pressure stamp with magnetic material and moving the pressure stamp longitudinal to the surface of the transplant in the bioreactor by a magnetic field or an electromagnetic field generated outside the bioreactor.

Claim 67 (new). The process according to claim 66, which comprises generating the magnetic field with at least one permanent magnet.

Claim 68 (new). The process according to claim 66, which comprises positioning at least two permanent magnets with alternating polarity on a mobile holder above the bioreactor and driving the holder by a servomotor in a cyclic manner, to thereby change a position thereof resulting in the pressure stamp applying pressure to the transplant alternately.

Claim 69 (new). The process according to claim 66, wherein the coil of an electromagnet alters, at a high frequency, a current direction and a voltage and therefore a field direction and a magnetic flow density through the bioreactor, whereby the pressure stamp applies pressure to the transplant alternately.

Claim 70 (new). A bioreactor for cultivating and stimulating three-dimensional, vital and mechanically resistant cell transplants in an GMP-conform bioreactor, the bioreactor comprising:

- a basic bioreactor body with a reactor lock connected thereto in a pressure-proof and sterile manner to define therein at least one reactor chamber;

- said reactor chamber having a support surface for a transplant formed therein and a mini actuator disposed therein; and

- at least two hose coupling connections for feeding and discharging of a medium or for gassing said reactor chamber.

Claim 71 (new). The device according to claim 70, wherein the reactor is a single-chamber bioreactor and the cell culture constructs are directly or indirectly cultivated and stimulated on a bioreactor floor of the single-chamber bioreactor.

Claim 72 (new). The device according to claim 70, wherein the reactor is a double-chamber bioreactor and the cell culture constructs are directly or indirectly, at least partially positioned on a floor of an upper reaction chamber of the double-chamber bioreactor for cultivation and stimulation, while the transplant is located in a second reactor chamber.

Claim 73 (new). The device according to claim 72, which comprises a transplant insert on the floor of the upper reactor chamber for receiving therein the cell constructs.

Claim 74 (new). The device according to claim 70, wherein said basic reactor body is a cylinder-shaped corpus closed from above with said reactor lock.

Claim 75 (new). The device according to claim 70, wherein said reactor lock is one or more reactor lock units connected to said bioreactor by one threaded joint and at least one conical nipple such that a threaded joint is either created between the reactor lock and the container(1) by a female thread in the container and a male thread in the reactor lock working together or the threaded joint is created between the reactor lock and the container in that a male thread in the container and a female thread in the reactor lock work together.

Claim 76 (new). The device according to claim 70, wherein said reactor lock is a cover equipped with biosensors and/or measuring heads.

Claim 77 (new). The device according to claim 76, wherein said cover is equipped with a sample taking section.

Claim 78 (new). The device according to claim 71, wherein said basic body of said single-chamber bioreactor has at least two each of a feed and discharge borehole for hose coupling connections.

Claim 79 (new). The device according to claim 78, wherein said feed connections and discharge connections communicating with said bioreactor chamber are fitted with a 3-way valve or a 4-way valve with a return function.

Claim 80 (new). The device according to claim 79, wherein at least one of said discharge connections is formed with a sample taking section.

Claim 81 (new). The device according to claim 72, wherein said basic body of said double-chamber bioreactor has at least two boreholes for hose coupling connections.

Claim 82 (new). The device according to claim 81, wherein at least one hose coupling connection is integrated in a lower reaction chamber and at least one is integrated in an upper reaction chamber.

Claim 83 (new). The device according to claim 82, wherein said hose coupling connections communicating with said bioreactor chamber are fitted with a 3-way valve or a 4-way valve with a return function.

Claim 84 (new). The device according to claim 83, wherein at least one of said discharge connections is formed with a sample taking section.

Claim 85 (new). The device according to claim 70, wherein the bioreactor has a reactor floor of a completely or partially transparent material for monitoring the transplant manufacture.

Claim 86 (new). The device according to claim 70, which comprises a foil, a fleece or a membrane of an antistatic or inert material disposed above the reactor floor of the bioreactor for the positioning of the transplant.

Claim 87 (new). The device according to claim 86, wherein the material for positioning the transplant is wide-meshed and light, fluid and gas permeable.

Claim 88 (new). The device according to claim 72, wherein the upper reactor chamber of said double-chamber bioreactor has an area corresponding to a transplant area while the dimensions of the lower chamber are less than those of the transplant so that if a cell culture is placed medially, the construct is mainly positioned underneath the lower chamber and lies partially on the reactor floor of

the upper chamber.

Claim 89 (new). The device according to claim 88, wherein the space underneath the reactor chamber is filled out by a flat plate of a biologically inert, light-permeating, wide-pored material, said plate being flush with the floor of the upper reactor chamber.

Claim 90 (new). The device according to claim 89, wherein said plate is formed of a porous sinter material.

Claim 91 (new). The device according to claim 89, wherein a foil, fleece or membrane of an antistatic or inert material for positioning the transplant disposed above the lower reactor chamber that is filled out by said plate on the reactor floor of the upper reactor chamber of said double-chamber bioreactor.

Claim 92 (new). The device according to claim 91, wherein said material is wide-meshed and permeable to light, fluid and gas.

Claim 93 (new). The device according to claim 89, wherein the components underneath the transplant in said double-chamber bioreactor, including the transparent plate, the lower chamber with the inserted porous material and a wide-meshed membrane have an overall height not exceeding a focal distance of conventional microscopes and camera objectives.

Claim 94 (new). The device according to claim 70, wherein said mini actuator comprises a magnetic piston-type actuator disposed in said bioreactor and movable through said bioreactor under control of one or more externally disposed control and steering magnets.

Claim 95 (new). The device according to claim 71, wherein said mini actuator in said single-chamber bioreactor is situated above said membrane and the transplant in said bioreactor chamber.

Claim 96 (new). The device according to claim 72, wherein said mini actuator in said double-chamber bioreactor is situated in the upper reactor space above a porous material, above a membrane and the transplant.

Claim 97 (new). The device according to claim 94, wherein said magnetic mini actuator is formed of a magnetic core encapsulated in a biologically inert enveloping body.

Claim 98 (new). The device according to claim 97, wherein said magnetic core is oriented to cause a field generated thereby between the poles runs vertically to the transplant, with a magnetic north pole of said mini actuator oriented in an upward direction.

Claim 99 (new). The device according to claim 97, wherein said enveloping body is a biocompatible enveloping body surrounding said core and having an external form matching a form of the reactor chamber of the bioreactor.

Claim 100 (new). The device according to claim 97, wherein a complete height of said enveloping body is such that a placement of said mini actuator in the reactor space results in a vertically-oriented guiding of a pressure stamp of said mini actuator towards the transplant.

Claim 101 (new). The device according to claim 97, wherein said mini-actuator is a piston-shaped mini actuator comprising a plurality of enveloping body cylinders, with one of said enveloping body cylinders containing the encapsulated permanent magnet and an additional cylinder serving the stamp impression, and a bridge connection joining the spatially separated cylinders.

Claim 102 (new). The device according to claim 97, wherein a planar stamp surface on an underside of said mini actuator formed by said enveloping body runs vertical to a guide direction in the bioreactor space.

Claim 103 (new). The device according to claim 97, wherein a stamp surface of said mini actuator has organotypical negative forms embossed thereon.

Claim 104 (new). The device according to claim 97, wherein a planar or formed stamp surface is embossed with a grid structure for increasing a stamp surface.

Claim 105 (new). The device according to claim 97, wherein said enveloping body of said mini actuator is formed with drill holes and/or flow channels guaranteeing a continued exact vertical guiding of said mini actuator at at least three locations of the periphery.

Claim 106 (new). The device according to claim 97, wherein the stamp surface of the mini actuator is fitted with at least one nosepiece which slides into its exactly fitting integrated guide rail in the bioreactor body.

Claim 107 (new). The device according to claim 97, wherein a control and steering magnet disposed outside the bioreactor brings about an oriented movement of said mini actuator with the magnetic or electro-magnetic field which it generates with the north pole of the permanent magnet that is oriented upwards.

Claim 108 (new). The device according to claim 97, wherein a control and steering magnet is medially situated in a vertical axis to the pressure stamp, preferably above the pressure stamp and moves upwards and downwards in relation to the polarity of the mini actuator, resulting in an alteration of the pressure applied to the transplant.

Claim 109 (new). The device according to claim 94, wherein said control and steering magnet comprises two permanent magnets with different vertical magnetic pole directions which are inserted in a rectangular shaped magnet holder and moved to their horizontal position above the bioreactor in a cyclic manner by means of a servomotor and a guide rail.

Claim 110 (new). The device according to claim 94, wherein said control and steering magnet comprises a minimum of two permanent magnets with different vertical magnetic pole directions, said permanent magnets being in a disk-shaped magnet holder and moved over the bioreactor in a cyclic manner as a result of the rotation drive of a servomotor.

Claim 111 (new). The device according to claim 110, wherein the bioreactors which are firmly fixed in their horizontal position approach the permanent magnets via a vertical movement of the magnet holder by way of a step motor, in order to increase a field effect and generate an application of higher pressures on the transplant.

Claim 112 (new). The device according to claim 111, wherein at least two bioreactors are so arranged in a station that their mini actuators are driven by just one permanent magnetic control system in a contactless manner.

Claim 113 (new). The device according to claim 94, wherein said control and steering magnet is an electromagnet with at least one induction coil with an infinitely variable field.

Claim 114 (new). The device according to claim 113, wherein said induction coil is highly frequently triggered by frequencies which can be altered in order to generate high-dynamic magnetic field alterations and mini actuator movement on the transplant.

Claim 115 (new). The device according to claim 70, which comprises a seeding piston with an inside diameter corresponding to an outside diameter of the transplants is disposed on a moving sliding plate for injecting the cells and the carrier matrix.

Claim 116 (new). The device according to claim 115, wherein said moving sliding

plate and the inside of the seeding piston are coated by an inert membrane, foil or polymer fleece.

Claim 117 (new). The device according to claim 115, wherein an exactly fitting stamp with a planar stamp surface or an organotypical negative form in the seeding piston is lightly applied to a cell suspension.

Claim 118 (new). The device according to claim 115, wherein an outside diameter of said seeding piston exactly matches an inside diameter of said bioreactor.

Claim 119 (new). The device according to claim 70, wherein at least three fixation walls are integrated in the reactor floor of said bioreactor, said fixation walls having dimensions for accommodating a transplant insert and to not impair a pressure compression of the transplant.